The ecology of wildlife disease surveillance: demographic and prevalence fluctuations undermine surveillance

Walton, L; Marion, G; Davidson, RS; White, PCL; Smith, LA; Gavier-Widen, D; Yon, L; Hannant, D; Hutchings, MR

Published in:
Journal of Applied Ecology

DOI:
10.1111/1365-2664.12671

Print publication: 01/10/2016

Document Version
Publisher's PDF, also known as Version of record

Journal of Applied Ecology

British Ecological Society

Journal of Applied Ecology 2016, **53,** 1460–1469 doi: 10.1111/1365-2664.12671

The ecology of wildlife disease surveillance: demographic and prevalence fluctuations undermine surveillance

Laura Walton[1,2,3], Glenn Marion[1]*, Ross S. Davidson[2], Piran C.L. White[3], Lesley A. Smith[2], Dolores Gavier-Widen[4], Lisa Yon[5], Duncan Hannant[5] and Michael R. Hutchings[2]

[1]*Biomathematics and Statistics Scotland, James Clerk Maxwell Building, The King's Buildings, Peter Guthrie Tait Road, Edinburgh EH9 3FD, UK;* [2]*Disease Systems Team, SRUC, King's Buildings, West Mains Road, Edinburgh EH9 3JG, UK;* [3]*Environment Department, Wentworth Way, University of York, York YO10 5NG, UK;* [4]*Department of Biomedical Science and Veterinary Public Health, Swedish University of Agricultural Sciences, Box 7028, 75007 Uppsala, Sweden; and* [5]*School of Veterinary Medicine and Science, University of Nottingham, Sutton Bonington Campus, Leicestershire LE12 5RD, UK*

Summary

1. Wildlife disease surveillance is the first line of defence against infectious disease. Fluctuations in host populations and disease prevalence are a known feature of wildlife disease systems. However, the impact of such heterogeneities on the performance of surveillance is currently poorly understood.

2. We present the first systematic exploration of the effects of fluctuations' prevalence and host population size on the efficacy of wildlife disease surveillance systems. In this study, efficacy is measured in terms of ability to estimate long-term prevalence and detect disease risk.

3. Our results suggest that for many wildlife disease systems, fluctuations in population size and disease lead to bias in surveillance-based estimates of prevalence and overconfidence in assessments of both the precision of prevalence estimates and the power to detect disease.

4. Neglecting such ecological effects may lead to poorly designed surveillance and ultimately to incorrect assessments of the risks posed by disease in wildlife. This will be most problematic in systems where prevalence fluctuations are large and disease fade-outs occur. Such fluctuations are determined by the interaction of demography and disease dynamics. Although particularly likely in highly fluctuating populations typical of fecund short-lived hosts, such fluctuations cannot be ruled out in more stable populations of longer-lived hosts.

5. *Synthesis and applications*. Fluctuations in population size and disease prevalence should be considered in the design and implementation of wildlife disease surveillance, and the framework presented here provides a template for conducting suitable power calculations. Ultimately, understanding the impact of fluctuations in demographic and epidemiological processes will enable improvements to wildlife disease surveillance systems leading to better characterization of, and protection against endemic, emerging and re-emerging disease threats.

Key-words: demographic fluctuations, disease surveillance, disease transmission models, stochastic population models, wildlife disease systems, wildlife ecology, wildlife populations

Introduction

Surveillance is the first line of defence against disease, whether to monitor endemic cycles of infection (Ryser-Degiorgis 2013) or to detect incursions of emerging or re-emerging diseases (Kruse, Kirkemo & Handeland 2004; Lipkin 2013). Identification and quantification of disease presence and prevalence is the starting point for developing disease control strategies as well as monitoring their efficacy (OIE 2013). Knowledge of disease in wildlife is of considerable importance for managing risks to humans (Daszak, Cunningham & Hyatt 2000; Jones *et al.* 2008) and livestock (Gortázar *et al.* 2007), as well as for the

*Correspondence author. E-mail: glenn@bioss.ac.uk

conservation of wildlife species themselves (Daszak, Cunningham & Hyatt 2000).

Recent public health concerns, for example highly pathogenic avian influenza (Artois *et al.* 2009b), alveolar echinococcosis (Eckert & Deplazes 2004) and West Nile Virus (WNV; Brugman *et al.* 2013), have led to a growing recognition that current approaches need to be improved (Mörner *et al.* 2002). For example, there is no agreed wildlife disease surveillance protocol shared among the countries in the European Union (Kuiken *et al.* 2011). Furthermore, several authors have identified the need for improvements to the structure, understanding and evaluation of wildlife disease surveillance (Bengis *et al.* 2004; Gortázar *et al.* 2007).

Much current practice for wildlife disease surveillance (Artois *et al.* 2009a) is based on ideas developed for surveillance in livestock, including calculation of sample sizes needed for accurate prevalence estimation (Grimes & Schulz 1996; Fosgate 2005) and detection of disease within a population (Dohoo, Martin & Stryhn 2005). A common feature of these methods is that they assume constant host populations and disease prevalence. These assumptions lead naturally to sample size calculations (for both disease detection and prevalence estimation) which are based on a binomial distribution and associated corrections for populations of finite size, such as the hypergeometric distribution (Artois *et al.* 2009a). Fosgate (2009) reviewed current approaches to sample size calculations in livestock systems and emphasized the importance of basing analyses on realistic assumptions about the system under surveillance.

Although constant population size and prevalence may often be reasonable assumptions for the analysis of livestock systems, they are considerably less tenable in wildlife disease systems, which are typically subject to much greater fluctuations in host population density and disease prevalence. Both sampling practicalities and changes in population density make it much harder to obtain a random sample of hosts of the desired sample size in wildlife disease surveillance programmes (Nusser *et al.* 2008), compared with livestock systems. It is not uncommon for wildlife disease surveillance to extend over several years and to test only a small fraction of the at-risk population. For example, McGarry and co-workers report overall prevalence of zoonotic helminths in 42 brown rats *Rattus norvegicus* captured in a programme of active surveillance carried out in an urban area in England between 2008 and 2011 (McGarry *et al.* 2014). These authors also present comparable results from several studies in Europe and North America, while another of the same host species conducted over a 2-year period across a broad area of north-western England captured just 133 individuals (Pounder *et al.* 2013). A notable example of passive surveillance, that is the testing of found dead individuals, is that for zoonotic WNV in wild birds across the whole of Great Britain during 2002–2009 in which only 2072 individuals representing 240 species were tested (Brugman *et al.* 2013).

The importance of temporal (Renshaw 1991; Wilson & Hassell 1997), spatial (Lloyd & May 1996; Tilman & Kareiva 1997) and other forms of heterogeneity (Read & Keeling 2003; Vicente *et al.* 2007; Davidson, Marion & Hutchings 2008) in population ecology has long been recognized (Anderson 1991; Smith *et al.* 2005), along with their role in the dynamics and persistence of infectious disease (Fenton *et al.* 2015). Detailed field observations have provided valuable insights into the temporal dynamics of wildlife disease systems. For example, a study (Telfer *et al.* 2002) of cowpox virus in two rodent host species at two sites over a 4-year period reveals strong temporal fluctuations in both population size and disease prevalence including disease fade-out (local extinction and re-emergence). Fade-outs are also observed in wildlife populations of longer-lived mammals as shown by a 6-year study (Hawkins *et al.* 2006) of devil facial tumour disease in *Sarcophilus harrisii* Tasmanian devil. One of the longest running and most intensive studies of disease in wildlife is the surveillance from 1982 to the present of TB in badgers at Woodchester Park, England, where around 80% of the population is trapped tested and released annually (Delahay *et al.* 2000). These long-term observations have revealed important insights into the dynamics of TB in badgers, for example that infection within social groups is persistent, whereas transmission between social groups is limited (Delahay *et al.* 2000). Parameter estimates derived from this study are used as a reference point for the simulation studies conducted below.

Despite these theoretical and empirical studies of temporal heterogeneities in wildlife disease systems, such effects have yet to be systematically accounted for, either in the design of surveillance programmes for wildlife disease systems, or in the analysis of the data obtained from them. Here, we address this gap by using a non-spatial simulation model of a wildlife host population, subject to demographic fluctuations and pathogen transmission, in order to explore the impact of stochastic fluctuations in host demography and disease dynamics on the performance of surveillance. Two measures of surveillance performance are considered: estimation of long-term prevalence and the ability (probability) to detect disease. Our results show that temporal fluctuations in wildlife disease systems limit the ability of surveillance to achieve both.

Materials and methods

We develop a generic modelling framework that represents key features of surveillance in wildlife disease systems including essential aspects of demography, disease dynamics and surveillance design. This framework is described below along with three simulation studies that enable us to explore the performance of surveillance across a wide range of scenarios representative of real-world systems.

STOCHASTIC MODELLING FRAMEWORK

The model represents a host population subject to demographic fluctuations (births, deaths and immigration) and the transmission of a single pathogen. At each point in time t, the state space represents the total population size $N(t)$, with $I(t)$ of these infected and $S(t) = N(t) - I(t)$ susceptible. The prevalence is then given by $p(t) = I(t)/N(t)$.

Demography

The birth rate of individuals is logistic, $rN(1 - N/k)$, with intrinsic growth rate r and carrying capacity k, reflecting the assumptions that population growth is resource-limited. Individuals have a per capita death rate μ, and immigration occurs at a constant rate ν.

Disease dynamics

A proportion γ of immigrants are infected, but otherwise all individuals enter the population (through birth or immigration) as susceptible, since we assume vertical and pseudo-vertical transmission are negligible. Susceptible individuals become infected at rate $\beta_0 S(t)$ through primary transmission (contact with infectious environmental sources including individuals outside the modelled population) and at rate $\beta S(t)I(t)$ by secondary transmission (contact with already infected individuals from within the population).

Disease surveillance

During a single period of surveillance (*surveillance bout*), individuals are captured at *per capita* rate α, tested and released, and both the total number, and the number of infected individuals caught are recoded. Perfect diagnostic tests are assumed although limited sensitivities and specificities could be accounted for. A surveillance bout continues until a defined sample size m is obtained or some upper time limit has been reached. Such surveillance is most naturally considered in the context of active capture campaigns but could also be adapted to samples obtained from hunting and passive surveillance by accounting for the losses and sources of bias associated with such surveillance methods (see, e.g. McElhinney *et al.* 2014).

Model implementation

The model framework is summarized in Table 1. Reported results are temporal averages (e.g. expected mean $E[N]$ and variance Var $[N]$ in population size) based on long-run simulations following a burn-in period to allow the population to reach equilibrium – where the effects of initial conditions are negligible. Within each run, repeated surveillance bouts are simulated and the probability of detection PD is estimated as the proportion of bouts where disease is detected. The mean $E[\hat{p}_{\text{surv}}]$ and variance $\text{Var}[\hat{p}_{\text{surv}}]$ of the prevalence estimates averaged over repeated bouts are also recorded. We consider a continuous state-space implementation simulated by numerically integrating a set of stochastic differential equations (SDEs) and a discrete state-space implementation using the Gillespie algorithm (see Appendix S1, Supporting information).

Table 1. Model structure

Event	Rate	Effect
Birth	$rN(1 - N/k)$	$S \to S + 1$
Death of susceptible	μS	$S \to S - 1$
Death of infected	μI	$I \to I - 1$
Susceptible immigration	$(1 - \gamma)\nu$	$S \to S + 1$
Infected immigration	$\gamma\nu$	$I \to I + 1$
Primary transmission	$\beta_0 S$	$S \to S - 1$ $I \to I + 1$
Secondary transmission	βIS	$S \to S - 1$ $I \to I + 1$
Susceptible active capture and release	αS	$S \to S$
Infected active capture and release	αI	$I \to I$

Event, rate and effect on the state space of the model. Conceptually, the effect of each event affects an individual and this is reflected in the discrete nature of the corresponding changes in the state space. However, given this underlying conception of the model, there are a number of different implementations which can be considered including via the Gillespie algorithm and stochastic differential equations (see text for details).

SIMULATION STUDIES

Study 1 (results shown in Figs 1 and 3) uses the SDE implementation and is designed to explore a generic but representative range of wildlife disease systems. Simulations were run for four values (0·01, 0·04, 0·1, 1·0) of the secondary transmission rate β. In each case, the population death rate μ was varied over a wide range between 0·1 and 0·5, with the intrinsic growth rate set at $r = 0{\cdot}5$ so that, at the upper end of this range, populations are highly unstable. This gives rise to typical population sizes of 10–40 (see Fig. 1a) and a wide range of disease prevalence. Similar results are obtained from simulations (not shown) where β is varied for a set of fixed values of μ where mortality rates span the interval $(0, r)$. Simulations not included here show that our results generalize, holding for transmission rates relative to a recovery rate (governing an additional transition from I to S) and death rates relative to birth rate, r. Different intensities of surveillance were simulated using four capture rates α (0·01, 0·1, 1·0, 10), for a sample size $m = 10$. Full parameterizations for Figs 1 and 3 are shown in Tables S3 and S6 in Appendix S2, respectively.

Study 1a (results shown in Fig. 2) explores the effect of surveillance design using a subset of the parameter sets considered in study 1, namely $(\beta, \mu) = :$ (1·0, 0·43); (1·0, 0·4); and (0·1, 0·43). For each, a range of capture rates $\alpha = 0 \ldots 10$ (with $m = 10$) and a range of sample sizes $m = 1, \ldots, 10\,000$ (with $\alpha = 0{\cdot}1$) are considered. The values of all model parameters used are shown in Tables S4 and S5 in Appendix S2.

Relevance to real wildlife disease systems. The intrinsic annual growth and death rates for badgers have been estimated as $r = 0{\cdot}6$ and $\mu = 0{\cdot}4$ (Anderson & Trewhella 1985). Rescaling for $r = 0{\cdot}5$ as used in simulation study 1 corresponds to a rescaled $\mu = 0{\cdot}33$. In addition, the secondary transmission rate for TB in badger populations was been estimated by the same authors to be $\beta = 0{\cdot}06$–$0{\cdot}08$ assuming a density of badgers necessary for disease persistence is ~5 badgers km^{-2} (Anderson & Trewhella 1985). The population size considered in simulation study 1

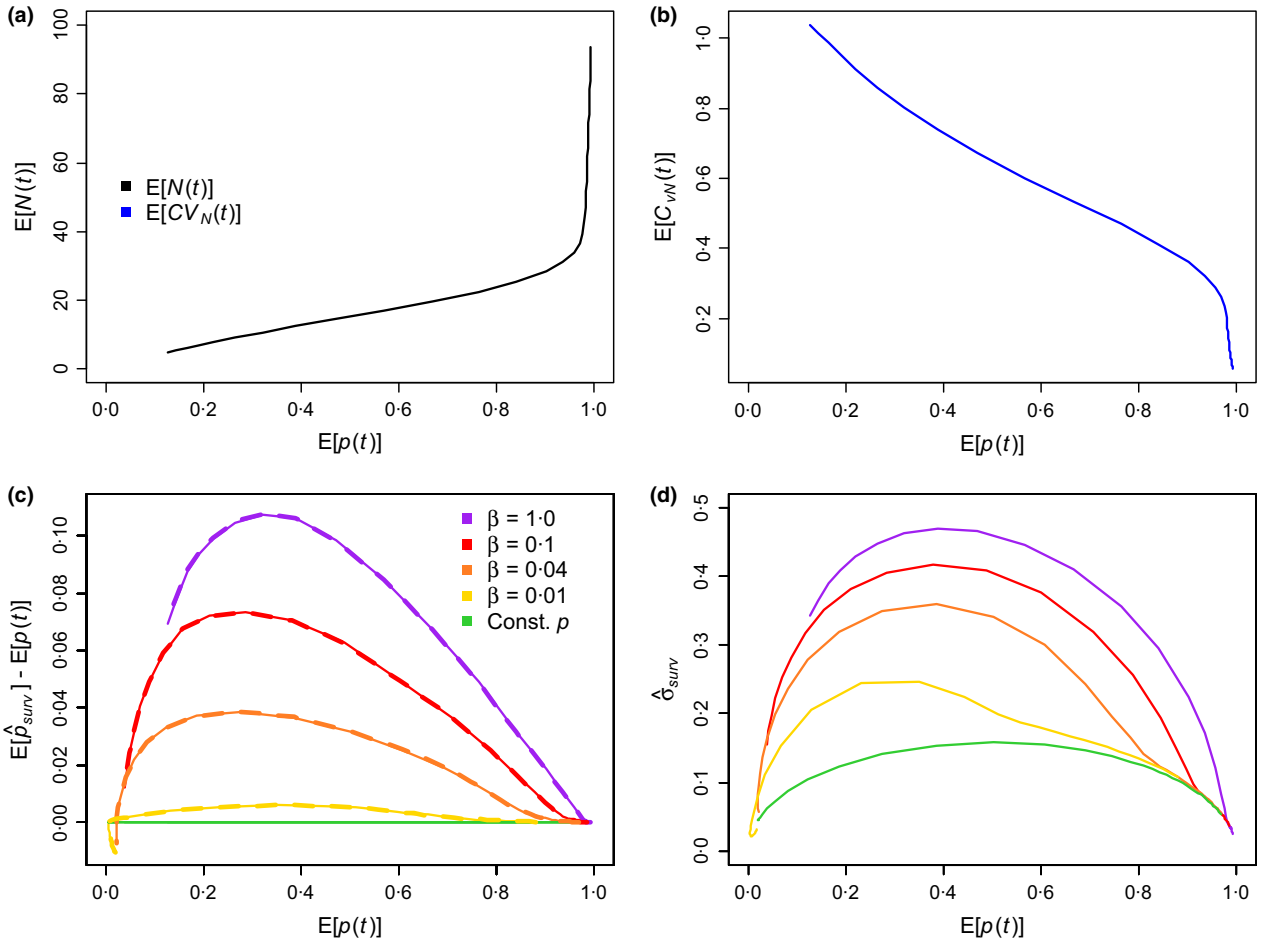

Fig. 1. Effect of host demography and disease transmission. Data are shown for a range of values of the death rate μ which controls the stability and size of the population and thus determines disease prevalence for a given transmission rate, β. For β = 1, plot (a) shows that expected population size increases with expected prevalence $E[p(t)]$ (i.e. as μ decreases) while (b) shows that the coefficient of variation of the population size decreases. For the four values of β indicated and fixed sample size $m = 10$, (c) shows the bias $E[\hat{p}_{surv}] - E[p(t)]$ and (d) the standard deviation in surveillance estimates of prevalence vs. the expected value of true disease prevalence in the system, $E[p(t)]$. Results shown are based on 10^6 surveillance bouts using the stochastic differential equation implementation of the model using the set of parameter values described in Appendix S2.

therefore corresponds to a surveillance area of around 8 km^2. The range of parameters considered in study 1 places badgers towards the stable end of the spectrum. More fecund and shorter-lived species would be expected to be less stable, for example have higher mortality and secondary transmission rates. As noted earlier, surveillance of badgers at Woodchester Park is relatively intensive leading to an annual probability of capture of around 80% corresponding to capture rates of $\alpha = 1{\cdot}6$–$2{\cdot}2$ (Delahay *et al.* 2000). The population of *Sarcophilus harrisii* Tasmanian devil discussed earlier consisted of between 20 and 60 individuals and was subject to annual capture rates between 0·5 and 1·7 (Hawkins *et al.* 2006). Estimates of capture rates are not available for the larger-scale studies referred to in the introduction (Brugman *et al.* 2013; Pounder *et al.* 2013; McGarry *et al.* 2014), but given the sample sizes obtained and the temporal and geographic scales involved, it seems reasonable to assume that they are considerably lower. Simulation study 1 encompasses a wide range of real-world wildlife disease surveillance.

Study 2 (results shown in Fig. 4) is designed to test the robustness of study 1 by exploring a wider range of scenarios: with intrinsic growth rates in the range (0,23); mortality rates in the range (0·25,14), carrying capacities in the range (0,36) and secondary contact rates in the range (0·01,5). Focussed on disease detection, results are conditioned on the presence of disease and simulations based on the Gillespie implementation, which explicitly handles the discrete nature of small populations. The values of all model parameters used in Fig. 4 are shown in Table S7 in Appendix S2.

Results

ESTIMATING PREVALENCE

In order to develop an understanding of the properties of wildlife disease surveillance using the above model, we developed expressions describing prevalence estimates obtained by continuous surveillance, that is continuously deployed effort resulting in per capita capture rate α.

Consider the interval $[0, T]$ during which the population history is $\mathcal{H}[0, T] = \{(N(t),p(t)): t \in [0, T]\}$, where $N(t)$

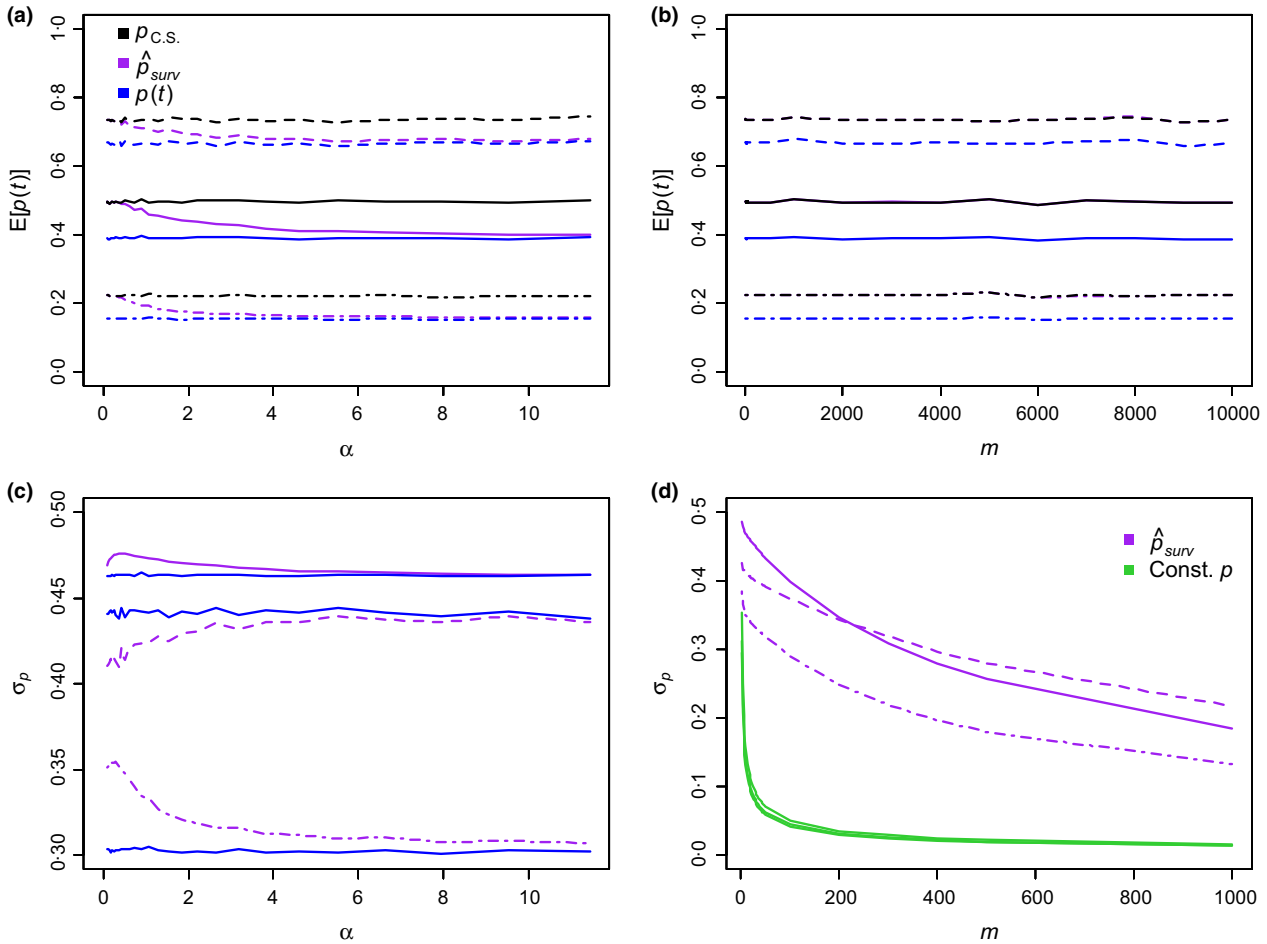

Fig. 2. Effect of surveillance design. In all plots, results are shown for three wildlife disease systems with (β, μ): (1, 0·43) solid lines, (1, 0·4) dashed and (0·1, 0·43) dot dashed. (a) and (b) show expected values of the surveillance estimate of prevalence (purple), the true prevalence (blue) and the continuous sampling theory prediction (black). (c) and (d) show the expected standard deviation (denoted, σ_p) in both the true (blue) and the surveillance estimated (purple) prevalence. (a) and (c) are plotted against a range of values of the capture rate α, for $m = 10$, and (b) and (d) vs. a range of sample sizes m for $\alpha = 0{\cdot}1$. (d) also shows the constant prevalence estimate of the standard deviation based on the binomial (green). Parameter values used are as described in Table S3.

and $p(t)$ represent the population size and disease prevalence at time $t \in [0, T]$, respectively (see above). Let n_T represent the total number, and i_T the number of infected individuals sampled during this time interval. Conditional on the history $\mathcal{H}[0, T]$, the expectations of these quantities are as follows:

$$E[n_T|\mathcal{H}[0,T]] = \int_0^T \alpha N(t)\mathrm{d}t \quad \text{and}$$

$$E[i_T|\mathcal{H}[0,T]] = \int_0^T \alpha N(t)p(t)\mathrm{d}t.$$

The surveillance estimate of disease prevalence is simply the ratio $\hat{p}_{surv}(T) = i_T/n_T$. Since immigration prevents extinction of the population and disease, then the long time limit of this estimate can be equated with its expectation over all histories as follows:

$$\lim_{T\to\infty}\hat{p}_{surv}(T) = E[\hat{p}_{surv}] = \lim_{T\to\infty}\frac{\frac{1}{T}\int_0^T N(t)p(t)\mathrm{d}t}{\frac{1}{T}\int_0^T N(t)\mathrm{d}t} = \frac{E[N(t)p(t)]}{E[N(t)]}.$$

This can be re-expressed in the more suggestive form:

$$E[\hat{p}_{Surv}] = E[p(t)] + \frac{\mathrm{Cov}[N(t),p(t)]}{E[N(t)]} \qquad \text{eqn 1}$$

Thus, when the covariance $\mathrm{Cov}[N(t),p(t)] = E[N(t)p(t)] - E[N(t)]E[p(t)]$ between the population size and the prevalence is nonzero, the surveillance estimate of prevalence is a biased estimate of the true prevalence, $E[p(t)]$. Since $\mathrm{Cov}[N(t),p(t)]$ will be zero when either $N(t)$ or $p(t)$ are constant, we conclude that demographic fluctuations and stochasticity in disease dynamics undermine the efficacy of surveillance.

Effect of host demography and disease dynamics

Figure 1 is based on simulation study 1 (see Materials and methods) and illustrates how population fluctuations and disease dynamics in the host–pathogen system affect the bias and variance of estimated prevalence. These results are generated by simulating the system, in each case until it reaches equilibrium, for a range of values of the death rate μ, with other parameters fixed. As the death rate increases, the equilibrium-expected population size decreases and the relative size of the population fluctuations increase as measured by the coefficient of variation. For a given rate of disease transmission β, increasing the death rate reduces expected prevalence, and therefore, simulating for different values of μ generates the range of prevalence values shown. The resulting relationship between demography and expected prevalence for particular disease characteristics (here a fixed transmission rate, β) is illustrated in Fig. 1a,b. These figures show increasing population size and lower demographic fluctuations as expected prevalence increases (i.e. as μ decreases).

Figure 1c shows the bias in the surveillance estimate of prevalence $E[\hat{p}_{\text{surv}}] - E[p(t)]$ obtained from the same set of simulations. Results shown are based on 10^6 surveillance bouts with sample size $m = 10$. The bias predicted by continuous sampling theory (which does not account for sample size) is also shown, and in this case, it accurately predicts simulated bias. Figure 1c shows the bias in surveillance estimates of prevalence for four different transmission rates. For a given prevalence, populations associated with higher transmission rate (β) are more variable than those with lower transmission rate, and therefore, Fig. 1c shows that such variability increases the bias of surveillance estimates of disease prevalence. Figure 1d shows the standard deviation in surveillance estimates of prevalence obtained from the same set of simulations. Comparison with the variability in prevalence estimates expected under the zero fluctuation assumption reveals that fluctuations in our simulated wildlife disease system reduce the precision (increase the variance) of estimates obtained by surveillance. The variability of these estimates also increases with demographic fluctuations. Thus, in terms of prevalence estimation, the dynamics of the host–pathogen interaction are integral in determining the efficacy of surveillance. Assessment for a given system would require parameterization of demography and disease dynamic, but the bias and variance in prevalence estimates shown in Fig. 1 are representative of a wide range of wildlife disease systems (see Materials and methods).

Additional studies shown in Appendix S2 confirm that the qualitative impact of fluctuations in population and the prevalence seen in Fig. 1 are robust to sample and population size and mode of secondary transmission. Figure S1 in Appendix S3 shows analogous results with sample size 100, where environmental variability drives fluctuations in a population around 100 times larger than considered above. Figure S3 in Appendix S3 shows results for simulation study 1 but where secondary transmission is frequency- (as opposed to density) dependent. Figure S5 and S6 in Appendix S3 show results from simulation study 1 with sample sizes 20 and 50, respectively.

Surveillance design

Based on simulation study 1a, Fig. 2 shows how the bias and variance of the estimate of prevalence changes as the intensity of surveillance (measured by the capture rate α) increases for fixed sample size (Fig. 2a,c), and as the sample size, m, increases for a fixed capture rate (Fig. 2b,d). For low capture rates, as $\alpha \to 0$ (and based on a fixed sample size), the continuous sampling estimate given in eqn 1 provides an accurate prediction for the level of prevalence estimated from surveillance. As shown above, this is a biased estimate of the true prevalence $E[p(t)]$. However, increasing the capture rate reduces bias, and as α increases, this bias tends to zero. In addition, for large capture rates, the precision of the surveillance estimate of prevalence matches the variability of the underlying wildlife disease system (see Fig. 2c). Thus, for low capture rates, the bias in surveillance estimates of prevalence is well described by continuous sampling theory (eqn 1). However, for larger capture rates, the properties of the surveillance estimate of prevalence increasingly reflect both the expected true prevalence (i.e. bias reduces) and the variability in the prevalence of the underlying disease system. In contrast, increasing sample size improves precision, but not bias (Fig. 2b). In comparison with the predictions from the standard binomial approach (which neglects fluctuations), these have lower precision and improve less quickly with increasing sample size (see Fig. 2d). Additional simulation results (not shown) indicate that as the sample size increases, the capture rate required to obtain unbiased estimates increases. However, even for large sample sizes, when sampling is instantaneous (i.e. $\alpha \to \infty$), the bias is zero and the standard deviation in the surveillance estimate of prevalence corresponds to that of the underlying wildlife disease system as shown above.

We previously noted that capture rates for relatively intensely monitored populations (Delahay *et al.* 2000; Hawkins *et al.* 2006) were between 0·5 and 2·2 with those of larger-scale studies (Brugman *et al.* 2013; Pounder *et al.* 2013; McGarry *et al.* 2014) lower still. Therefore, the results of Fig. 2 suggest fluctuations will lead to bias in surveillance-based estimates of prevalence for a wide range of wildlife disease systems. However, the size of these effects will be dependent on the details of host species demography and disease dynamics.

THE PROBABILITY OF DETECTION

If prevalence is assumed constant and equal to the long-term average prevalence $E[p]$ of the wildlife disease

system, then the probability that disease is detected in a sample of size m is given by:

$$\mathrm{PD}^{\mathrm{Bin}} = f(E[p], m) = 1 - (1 - E[p])^{\mathrm{m}} \qquad \text{eqn 2}$$

This formula, based on simple binomial arguments, and variants that also assume constant prevalence, are the standard basis for sample size calculations (see, e.g. Fosgate 2009). However, if prevalence fluctuates, $\mathrm{PD}^{\mathrm{Bin}}$ is a misleading estimate of the probability of detection.

When conducting surveillance, prevalence will vary between the times when each of the m samples is collected, but we assume prevalence within a given surveillance bout is constant and denote p. Figure 3a indicates that accounting only for fluctuations between surveillance bouts is an accurate approximation. Therefore, the expected probability of detection for sample size m is defined as

$$\mathrm{PD} = E[f(p, m)] = E[1 - (1 - p)^{m}] \qquad \text{eqn 3}$$

where the expectation is over the between-bout prevalence distribution $P(p)$ which accounts only for prevalence fluctuations between surveillance bouts. For a single sample $m = 1$, eqn 3 reduces to a linear form, so that $\mathrm{PD} = \mathrm{PD}^{\mathrm{Bin}} = E[p]$. However, if $m > 1$, then eqn 3 is non-linear, and therefore, $\mathrm{PD} \neq \mathrm{PD}^{\mathrm{Bin}}$. Further analysis of eqn 3, for example suggesting $\mathrm{PD} < \mathrm{PD}^{\mathrm{Bin}}$, is shown in Appendix S4.

Effect of host demography and transmission dynamics

The results shown in Fig. 3 demonstrate the effect of host demography, transmission dynamics and surveillance design on the probability of detection. These results are obtained from the simulations described in Fig. 1, except for those in Fig. 3d, where these simulations are rerun for

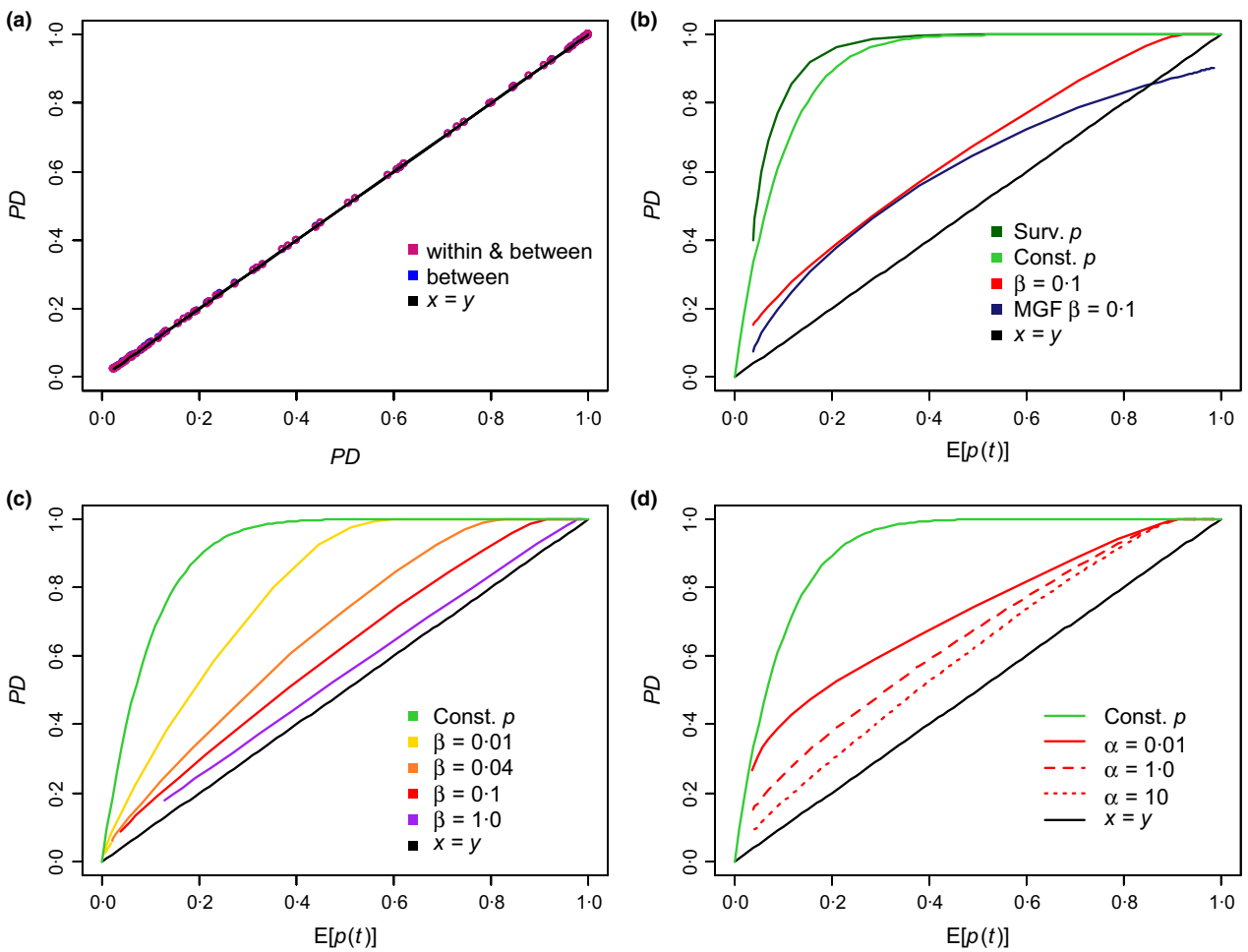

Fig. 3. Effect of host–pathogen and surveillance dynamics on probability of detection. Results based on simulations used for Fig. 1 (for details, see Table S4, Appendix S2). (d) estimated PD vs. approximations based on modifications of eqn 3 accounting for fluctuations in prevalence (i) within and between bouts and (ii) between bouts only. (c) shows $\mathrm{PD}^{\mathrm{Bin}}$ based on both $E[p]$ (green) and $E[\hat{p}_{\mathrm{surv}}]$ (black) and (for $\beta = 0{\cdot}1$) PD and the approximation (eqn 4) based on an assumed gamma distribution. (a) shows $\mathrm{PD}^{\mathrm{Bin}}$ (green) and PD for various values of β (as shown yellow ($\beta = 0{\cdot}01$), orange ($\beta = 0{\cdot}04$), red ($\beta = 0{\cdot}1$), purple ($\beta = 1{\cdot}0$)) vs. actual prevalence $E[p]$. (b) shows $\mathrm{PD}^{\mathrm{Bin}}$ (green) and PD for $\beta = 0{\cdot}1$ and the three capture rates $\alpha = 0{\cdot}01$, 1·0, 10. In (a), (b) and (c), the black line indicates $\mathrm{PD} = E[p(t)]$.

different values of the capture rate (see study 1a in Materials and methods).

Figure 3b illustrates an analytic calculation of PD based on approximating the between-bout prevalence distribution $P(p)$ as a gamma distribution (see Appendix S4). Although not completely successful, this does provide a more accurate prediction than PD^{Bin}. This approach could be used to improve sample size calculations in situations where simulation is not possible, but information about prevalence fluctuations is available. Moreover, the results of Fig. 3a show that such approximations could be improved by assuming a more accurate representation of the prevalence distribution $P(p)$. Crucially, these calculations support the conclusion that the true probability of detection is less than that obtained when ignoring fluctuations, that is less than PD^{Bin}. Figure 3b also shows the impact of biased prevalence estimation on disease detection for the case $\beta = 0{\cdot}1$. Figure 1 demonstrates that in this case, surveillance results in inflated estimates of prevalence $E[\hat{p}_{surv}] > E[p(t)]$. Ignoring the effect of fluctuations would therefore lead to an estimated detection probability greater than PD^{Bin}, which is based on the true average prevalence $E[p]$.

Figure 3c shows the effect of interactions between disease dynamics and demography. As in the case of prevalence estimation, conditioned on a given expected prevalence, larger contact rates β are associated with greater fluctuations in the underlying wildlife disease system (i.e. greater transmission rates are needed to sustain a given prevalence). Here, larger fluctuations translate into reduced probability of detection. In Fig. 3c, for $\beta = 1{\cdot}0$, the probability of detection is only a little above the line $PD = E[p]$; this corresponds to a single sample $m = 1$. Thus, in contrast to the zero fluctuation approximation PD^{Bin}, fluctuations reduce the effective sample size, for the $\beta = 1{\cdot}0$ case from $m = 10$ to close to $m = 1$. Results not shown indicate that the reduction in effective sample size increases with sample size (and see Fig. 4). Figure 3d shows the effect of capture rate on the probability of detection; counterintuitively, more intense surveillance effort actually reduces the probability of detection. This is consistent with the above observations regarding β; less intense effort means that the required sample size takes longer to gather, which reduces between-bout fluctuations in prevalence.

Limits to disease detection in wildlife disease systems

The nature of host demography and disease dynamics in wildlife disease systems will often be poorly understood especially in cases of emerging disease. Figure 4 is based on simulation study 2 (see Materials and methods) and shows the probability of detection associated with surveillance subject to demographic and disease fluctuations and the zero fluctuation approximation PD^{Bin}. This is done for two different sampling levels, and across a broader range of wildlife disease systems than considered above, each represented by one of the points on the graph. Depending on the level of fluctuations in the system, the effective sample size can range from the actual number of samples taken to $m \approx 1$. These results suggest that, when designing surveillance, ignoring the effect of fluctuations could lead to studies that are underpowered in their ability to detect disease. These results are consistent with those of Fig. 3 based on the SDE implementation.

Discussion

This paper represents the first systematic exploration of the impact of pathogen transmission dynamics and

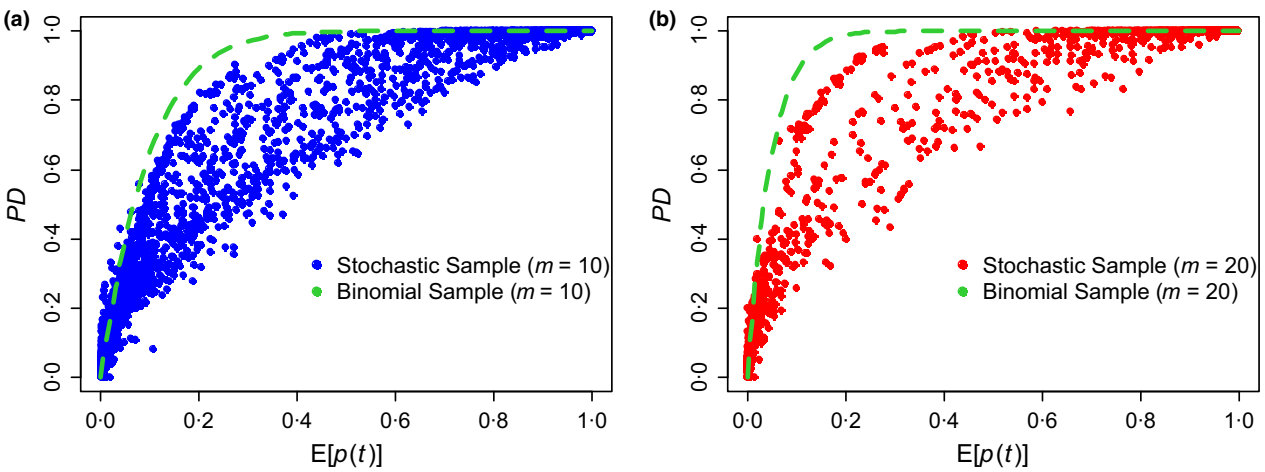

Fig. 4. Fluctuations reduce power to detect disease. The two panels show the probability that disease is detected (conditional on nonzero prevalence) for target sample sizes 10 and 20. Each coloured dot represents the average of 100–1000 realizations of the model implemented using the Gillespie algorithm that met the sample target for a particular combination of parameters representing a distinct host–pathogen system (for details, see Table S5, Appendix S2). The green dashed line in both graphs represents PD^{Bin} the probability of detection assuming constant prevalence (see eqn 2). It can be seen that PD^{Bin} generally overestimates the power of the sample in that it predicts a larger probability of detection than is realized in the stochastic simulations.

demographic aspects of host ecology on wildlife disease surveillance efficacy. We have introduced a framework within which surveillance design is characterized by the capture rate (α), in addition to the standard sample size (m). In this extended framework, the performance of surveillance is assessed in the light of the ecology of the wildlife disease system of interest, that is for particular population and disease parameters. The framework introduced here can thus serve as a template for performing power calculations that account for fluctuations in populations and disease prevalence for specific hosts and pathogens.

Our results show that surveillance design (choice of m and α) can have a large impact on bias and precision of prevalence estimation, and on the power to detect disease. With more unstable populations and greater fluctuations in disease, bias in prevalence estimates increases, and the precision of such estimates decreases. Such bias can be reduced by increasing capture rate, but for fixed sample size, this also reduces the ability to detect disease. However, results suggest that even in the most intensive wildlife disease surveillance programmes (Delahay *et al.* 2000; Hawkins *et al.* 2006), typical capture rates are not sufficient to eliminate bias. In contrast, increasing sample size does not affect bias, but does improve statistical power in terms of both precision of prevalence estimates and disease detection. However, as sample size increases, such improvements in power are not as fast as would be expected if fluctuations were ignored, as they are in current surveillance design and analysis (Grimes & Schulz 1996; Dohoo, Martin & Stryhn 2005).

Surveillance is a critical prerequisite for defining and controlling wildlife disease risks, and our results suggest that ignoring significant temporal fluctuations in the design of wildlife disease surveillance generates inadequate assessments of risk. Moreover, the ecology of many wildlife species and the pathogens to which they are exposed lead to significant temporal fluctuations in both population size and disease prevalence (Anderson & May 1979; Anderson 1991; Renshaw 1991; Wilson & Hassell 1997; Telfer *et al.* 2002; Hawkins *et al.* 2006). The studies reported here were designed to explore these effects in a wide range of scenarios representative of actual surveillance in wildlife disease systems (see Materials and methods), and suggest that such issues are likely to be widespread. A key aspect not accounted for in the work presented here is disease-induced mortality, which preliminary results (not shown) suggest is likely to accentuate the effects shown here. Moreover, frequency-dependent transmission and fluctuations driven by environmental variation, studied only briefly here, also reduced the efficacy of surveillance. The framework presented could also be extended to account for known extrinsic sources of bias, such as imperfect disease diagnostics, variation in habitat quality (Nusser *et al.* 2008; Walsh & Miller 2010) and biased capture rates (Tuyttens *et al.* 1999) including aspects associated with passive surveillance.

There is much current interest in quantifying risks from wildlife disease (Daszak, Cunningham & Hyatt 2000; Jones *et al.* 2008), and this is stimulating debate on the need to improve wildlife disease surveillance (Bengis *et al.* 2004; Butler 2006; Gortázar *et al.* 2007; Béneult, Ciliberti & Artois 2014). This paper will help to further inform this debate, highlighting the need to consider the ecology of wildlife disease systems when designing or analysing surveillance programmes (Béneult, Ciliberti & Artois 2014). This assessment emphasizes the importance of accounting for temporal heterogeneities induced by population fluctuations and disease dynamics. Further research is needed to assess the impacts of ecology on wildlife disease surveillance including alternative and complimentary heterogeneities such as intrinsic and extrinsic forms of spatial heterogeneity, and other population structures. There is a wealth of literature describing the effects of such heterogeneity in ecology and epidemiology (Lloyd & May 1996; Tilman & Kareiva 1997; Keeling, Wilson & Pacala 2000; Read & Keeling 2003; Keeling 2005; Vicente *et al.* 2007), and our results suggest that these are likely to have important, but as yet unexplored, impacts on the efficacy of wildlife disease surveillance.

Acknowledgements

This work was supported by the European Commission under the Food, Agriculture and Fisheries, and Biotechnology Theme of the 7th Framework Programme for Research and Technological Development, grant agreement no. 222633. GM, RSD, LAS and MRH are grateful for funding from the Scottish Government's RESAS. We are grateful to the referees whose comments helped to significantly improve the manuscript.

Data accessibility

Model code is available in Dryad Digital Repository doi: 10.5061/dryad.s6518 (Walton *et al.* 2016).

References

Anderson, R. (1991) Populations and infectious diseases: ecology or epidemiology? *The Journal of Animal Ecology*, **60**, 1–50.

Anderson, R. & May, R. (1979) Population biology of infectious diseases: Part I. *Nature*, **280**, 361–367.

Anderson, R.M. & Trewhella, W. (1985) Population dynamics of the Badger (*Meles meles*) and the epidemiology of bovine tuberculosis (*Mycobacterium bovis*). *Philosophical Transactions of the Royal Society B: Biological Sciences*, **310**, 327–381.

Artois, M., Bengis, R., Delahay, R.J., Duchêne, M.-J., Duff, J.P., Ferroglio, E. *et al.* (2009a) Wildlife disease surveillance and monitoring. *Management of Disease in Wild Mammals* (eds R.J. Delahay, G.C. Smith & M.R. Hutchings), pp. 187–213. Springer, Tokyo, Japan.

Artois, M., Bicout, D., Doctrinal, D., Fouchier, R., Gavier-Widen, D., Globig, A. *et al.* (2009b) Outbreaks of highly pathogenic avian influenza in Europe: the risks associated with wild birds. *Revue Scientifique et Technique (International Office of Epizootics)*, **28**, 69–92.

Béneult, B., Ciliberti, A. & Artois, M. (2014) A generic action plan against the invasion of the EU by an emerging pathogen in wildlife – a wildtech perspective. *Risk*, **2**, 174–181.

Bengis, R.G., Leighton, F.A., Fischer, J.R., Artois, M. & Mörner, T. (2004) The role of wildlife in emerging and re-emerging zoonoses. *Revue Scientifique et Technique (International Office of Epizootics)*, **23**, 497–511.

Brugman, V.A., Horton, D.L., Phipps, L.P., Johnson, N., Cook, A.J.C., Fooks, A.R. & Breed, A.C. (2013) Epidemiological perspectives on West Nile virus surveillance in wild birds in Great Britain. *Epidemiology and Infection*, **141**, 1134–1142.

Butler, D. (2006) Disease surveillance needs a revolution. *Nature*, **440**, 6–7.

Daszak, P., Cunningham, A.A. & Hyatt, A.D. (2000) Emerging infectious diseases of wildlife–threats to biodiversity and human health. *Science (New York, NY)*, **287**, 443–449.

Davidson, R.S., Marion, G. & Hutchings, M.R. (2008) Effects of host social hierarchy on disease persistence. *Journal of Theoretical Biology*, **253**, 424–433.

Delahay, R.J., Langton, S., Smith, G.C., Clifton-Hadley, R.S. & Cheeseman, C.L. (2000) The spatio-temporal distribution of *Mycobacterium bovis* (bovine tuberculosis) infection in a high-density badger population. *Journal of Animal Ecology*, **69**, 428–441.

Dohoo, I., Martin, W. & Stryhn, H. (2005) Veterinary epidemiologic research. *Preventive Veterinary Medicine*, **68**, 289–292.

Eckert, J. & Deplazes, P. (2004) Biological, epidemiological, and clinical aspects of echinococcosis, a zoonosis of increasing concern. *Clinical Microbiology Reviews*, **17**, 107–135.

Fenton, A., Streicker, D.G., Petchey, O.L., Pedersen, A.B., Fenton, A., Streicker, D.G., Petchey, O.L. & Pedersen, A.B. (2015) Are all hosts created equal? Partitioning host species contributions to parasite persistence in Multihost communities *The American Naturalist*, **186**, 610–622.

Fosgate, G.T. (2005) Modified exact sample size for a binomial proportion with special emphasis on diagnostic test parameter estimation. *Statistics in Medicine*, **24**, 2857–2866.

Fosgate, G.T. (2009) Practical sample size calculations for surveillance and diagnostic investigations. *Journal of Veterinary Diagnostic Investigation*, **21**, 3–14.

Gortázar, C., Ferroglio, E., Höfle, U., Frölich, K. & Vicente, J. (2007) Diseases shared between wildlife and livestock: a European perspective. *European Journal of Wildlife Research*, **53**, 241–256.

Grimes, D.A. & Schulz, K.F. (1996) Determining sample size and power in clinical trials: the forgotten essential. *Seminars in Reproductive Endocrinology*, **14**, 125–131.

Hawkins, C.E., Baars, C., Hesterman, H., Hocking, G.J., Jones, M.E., Lazenby, B. *et al.* (2006) Emerging disease and population decline of an island endemic, the Tasmanian devil *Sarcophilus harrisii*. *Biological Conservation*, **131**, 307–324.

Jones, K.E., Patel, N.G., Levy, M.A., Storeygard, A., Balk, D., Gittleman, J.L. & Daszak, P. (2008) Global trends in emerging infectious diseases. *Nature*, **451**, 990–993.

Keeling, M. (2005) The implications of network structure for epidemic dynamics. *Theoretical Population Biology*, **67**, 1–8.

Keeling, M.J., Wilson, H.B. & Pacala, S.W. (2000) Reinterpreting space, time lags, and functional responses in ecological models. *Science*, **290**, 1758–1761.

Kruse, H., Kirkemo, A.-M. & Handeland, K. (2004) Wildlife as source of zoonotic infections. *Emerging Infectious Diseases*, **10**, 2067–2072.

Kuiken, T., Ryser-Degiorgis, M.P., Gavier-Widen, D. & Gortázar, C. (2011) Establishing a European network for wildlife health surveillance. *Scientific and Technical Review*, **30**, 755–761.

Lipkin, W.I. (2013) The changing face of pathogen discovery and surveillance. *Nature Reviews Microbiology*, **11**, 133–141.

Lloyd, A.L. & May, R.M. (1996) Spatial heterogeneity in epidemic models. *Journal of Theoretical Biology*, **179**, 1–11.

McElhinney, L.M., Marston, D.A., Brookes, S.M. & Fooks, A.R. (2014) Effects of carcase decomposition on rabies virus infectivity and detection. *Journal of Virological Methods*, **207**, 110–113.

McGarry, J.W., Higgins, A., White, N.G., Pounder, K.C. & Hetzel, U. (2014) Zoonotic helminths of urban brown rats (*Rattus norvegicus*) in the UK: neglected public health considerations? *Zoonoses and Public Health*, **62**, 44–52.

Mörner, T., Obendorf, D.L., Artois, M. & Woodford, M.H. (2002) Surveillance and monitoring of wildlife diseases. *Revue Scientifique et Technique (International Office of Epizootics)*, **21**, 67–76.

Nusser, S.M., Clark, W.R., Otis, D.L. & Huang, L. (2008) Sampling considerations for disease surveillance in wildlife populations. *Journal of Wildlife Management*, **72**, 52–60.

OIE (2013) *Terrestrial Animal Health Code*. World Organisation for Animal Health, Paris. ISBN 978-92-9044-909-6.

Pounder, K.C., Begon, M., Sironen, T., Henttonen, H., Watts, P.C., Voutilainen, L. *et al.* (2013) Novel hantavirus in field vole, United Kingdom. *Emerging Infectious Diseases*, **19**, 673–675.

Read, J.M. & Keeling, M.J. (2003) Disease evolution on networks: the role of contact structure. *Proceedings of the Royal Society of London B: Biological Sciences*, **270**, 699–708.

Renshaw, E. (1991) *Modelling Biological Populations in Space and Time*. Cambridge University Press, Cambridge..

Ryser-Degiorgis, M.-P. (2013) Wildlife health investigations: needs, challenges and recommendations. *BMC Veterinary Research*, **9**, 223.

Smith, K.F., Dobson, A.P., Mckenzie, F.E., Real, L.A., Smith, D.L. & Wilson, M.L. (2005) Ecological theory to enhance infectious disease control and public health policy. *Frontiers in Ecology and the Environment*, **3**, 29–37.

Telfer, S., Bennett, M., Bown, K., Cavanagh, R., Crespin, L., Hazel, S., Jones, T. & Begon, M. (2002) The effects of cowpox virus on survival in natural rodent populations: increases and decreases. *Journal of Animal Ecology*, **71**, 558–568.

Tilman, D. & Kareiva, P. (1997) *Spatial Ecology: The Role of Space in Population Dynamics and Interspecific Interactions*. Princeton University Press, Princeton.

Tuyttens, F.A.M., Macdonald, D.W., Delahay, R., Rogers, L.M., Mallinson, P.J., Donnelly, C.A. & Newman, C. (1999) Differences in trappability of European badgers *Meles meles* in three populations in England. *Journal of Applied Ecology*, **36**, 1051–1062.

Vicente, J., Delahay, R., Walker, N. & Cheeseman, C.L. (2007) Social organization and movement influence the incidence of bovine tuberculosis in an undisturbed high-density badger Meles meles population. *Journal of Animal Ecology*, **76**, 348–360.

Walsh, D.P. & Miller, M.W. (2010) A weighted surveillance approach for detecting chronic wasting disease foci. *Journal of Wildlife Diseases*, **46**, 118–135.

Walton, L., Marion, G., Davidson, R.S., White, P.C.L., Smith, L.A., Gavier-Widen, D., Yon, L., Hannant, D. & Hutchings, M.R. (2016) Data from: The ecology of wildlife disease surveillance: demographic and prevalence fluctuations undermine surveillance. *Dryad Digital Repository*, http://dx.doi.org/10.5061/dryad.s6518.

Wilson, H.B. & Hassell, M.P. (1997) Host – parasitoid spatial models: the interplay of demographic stochasticity and dynamics. *Proceedings of the Royal Society of London, Series B: Biological Sciences*, **264**, 1189–1195.

Received 14 August 2015; accepted 4 April 2016
Handling Editor: Silke Bauer

Supporting Information

Additional Supporting Information may be found in the online version of this article.

Appendix S1. Model implementation.

Appendix S2. Parameterizations used.

Appendix S3. Additional scenarios.

Appendix S4. Analysis of disease detection probability.